

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID: SSSPTA1616BSK

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

NEWS 1	Web Page URLs for STN Seminar Schedule - N. America	
NEWS 2	"Ask CAS" for self-help around the clock	
NEWS 3	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 4	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 5	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 6	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 7	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 8	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 9	MAR 22	EMBASE is now updated on a daily basis
NEWS 10	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 11	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 12	APR 04	STN AnaVist \$500 visualization usage credit offered
NEWS 13	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 14	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 15	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected
NEWS 16	MAY 10	CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS 17	MAY 11	KOREAPAT updates resume
NEWS 18	MAY 19	Derwent World Patents Index to be reloaded and enhanced
NEWS 19	MAY 30	IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2
NEWS 20	MAY 30	The F-Term thesaurus is now available in CA/CAplus
NEWS 21	JUN 02	The first reclassification of IPC codes now complete in INPADOC
NEWS EXPRESS	FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT http://download.cas.org/express/v8.0-Discover/	
NEWS HOURS	STN Operating Hours Plus Help Desk Availability	
NEWS LOGIN	Welcome Banner and News Items	
NEWS IPC8	For general information regarding STN implementation of IPC 8	
NEWS X25	X.25 communication option no longer available after June 2006	

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

FILE 'HOME' ENTERED AT 16:51:57 ON 12 JUN 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.68	1.68

FILE 'REGISTRY' ENTERED AT 16:56:36 ON 12 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 11 JUN 2006 HIGHEST RN 887399-72-6
DICTIONARY FILE UPDATES: 11 JUN 2006 HIGHEST RN 887399-72-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

```
*****
* The CA roles and document type information have been removed from
* the IDE default display format and the ED field has been added,
* effective March 20, 2005. A new display format, IDERL, is now
* available and contains the CA role and document type information.
*****
*****
```

Structure search iteration limits have been increased. See **HELP SLIMITS** for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

```
=> Uploading C:\Program Files\Stnexp\Queries\spermire.str
```

L1 STRUCTURE UPLOADED

```
=> sss 11 full
SSS IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (>).
```

=> s sss 11 full
FULL SEARCH INITIATED 16:56:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 296340 TO ITERATE

100.0% PROCESSED 296340 ITERATIONS 7 ANSWERS
SEARCH TIME: 00.00.03

L2 7 SEA SSS FUL L1

=> file caplus biosis embase uspatfull
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 166.94 168.62

FILE 'CAPLUS' ENTERED AT 16:57:07 ON 12 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'BIOSIS' ENTERED AT 16:57:07 ON 12 JUN 2006

Copyright (c) 2006 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 16:57:07 ON 12 JUN 2006

Copyright (c) 2006 Elsevier B.V. All rights reserved.

FILE 'USPATFULL' ENTERED AT 16:57:07 ON 12 JUN 2006

CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

=> s 12

L3 17 L2

=> dup rem 13

PROCESSING COMPLETED FOR L3

L4 17 DUP REM L3 (0 DUPLICATES REMOVED)

=> d ibib abs hitstr 1-17

L4 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:163695 CAPLUS

DOCUMENT NUMBER: 144:384807

TITLE: Guide Molecule-driven Stereospecific Degradation of α -Methylpolyamines by Polyamine Oxidase

AUTHOR(S): Jaervinen, Aki; Keinaenen, Tuomo A.; Grigorenko, Nikolay A.; Khomutov, Alex R.; Uimari, Anne; Vepsaelainen, Jouko; Naervaenen, Ale; Alhonen, Leena; Jaenne, Juhani

CORPORATE SOURCE: A. I. Virtanen Institute for Molecular Sciences and the Department of Chemistry, University of Kuopio, Kuopio, FI-70211, Finland

SOURCE: Journal of Biological Chemistry (2006), 281(8), 4589-4595

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

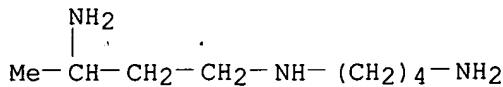
AB FAD-dependent polyamine oxidase (PAO; EC 1.5.3.11) is one of the key enzymes in the catabolism of polyamines spermidine and spermine. The natural substrates for the enzyme are N1-acetylspermidine, N1-acetylspermine, and N1,N12-diacetylspermine. Here we report that PAO, which normally metabolizes achiral substrates, oxidized (R)-isomer of 1-amino-8-acetamido-5-azanonane and N1-acetylspermidine as efficiently while (S)-1-amino-8-acetamido-5-azanonane was a much less preferred substrate. It has been shown that in the presence of certain aldehydes, the substrate specificity of PAO and the kinetics of the reaction are changed to favor spermine and spermidine as substrates. Therefore, we examined the effect of several aldehydes on the ability of PAO to oxidize different enantiomers of α -methylated polyamines. PAO supplemented with benzaldehyde predominantly catalyzed the cleavage of (R)-isomer of α -methylspermidine, whereas in the presence of pyridoxal the (S)- α -methylspermidine was preferred. PAO displayed the same stereospecificity with both singly and doubly α -methylated spermine derivs. when supplemented with the same aldehydes. Structurally related ketones proved to be ineffective. This is the first time that the stereospecificity of FAD-dependent oxidase has been successfully regulated by changing the supplementary aldehyde. These findings might facilitate the chemical regulation of stereospecificity of the enzymes.

IT 150333-68-9 878190-33-1 878190-34-2

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(guide mol.-driven stereospecific degradation of α -methylpolyamines by polyamine oxidase)

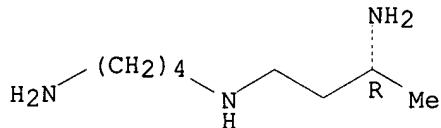
RN 150333-68-9 CAPLUS

CN 1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



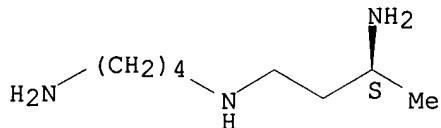
RN 878190-33-1 CAPLUS
 CN 1,3-Butanediamine, N1-(4-aminobutyl)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 878190-34-2 CAPLUS
 CN 1,3-Butanediamine, N1-(4-aminobutyl)-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

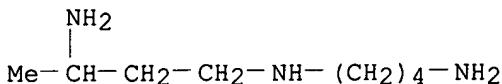


REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1306975 CAPLUS
 DOCUMENT NUMBER: 144:212934
 TITLE: α -Methyl Polyamines: Efficient Synthesis and Tolerance Studies in Vivo and in Vitro. First Evidence for Dormant Stereospecificity of Polyamine Oxidase
 JAERVINEN, Aki J.; CERRADA-GIMENEZ, Marc; GRIGORENKO, Nikolay A.; KHOMUTOV, Alex R.; VEPSAELAELINEN, Jouko J.; SINERVIRTA, Riitta M.; KEINAENEN, Tuomo A.; ALHONEN, Leena I.; JAENNE, Juhani E.
 AUTHOR(S): Department of Biotechnology and Molecular Medicine, A.I. Virtanen Institute for Molecular Sciences, and Department of Chemistry, University of Kuopio, Kuopio, Finland
 CORPORATE SOURCE: Journal of Medicinal Chemistry (2006), 49(1), 399-406
 SOURCE: CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 144:212934
 AB Efficient syntheses of metabolically stable α -methylspermidine, α -methylspermine, and bis- α, α' -methylated spermine starting from Et 3-aminobutyrate are described. The biol. tolerance for these compds. was tested in wild-type mice and transgenic mice carrying the metallothionein promoter-driven spermidine/spermine N1-acetyltransferase gene (MT-SSAT). The efficient substitution of natural polyamines by their derivs. was confirmed in vivo with the rats harboring the same MT-SSAT transgene and in vitro with the immortalized fibroblasts derived from these animals. Enantiomers of previously unknown 1-amino-8-acetamido-5-azanonane dihydrochloride (I) were synthesized starting from enantiomerically pure (R)- and (S)-alaninols. The studies with recombinant human polyamine oxidase (PAO) showed that PAO (usually splits achiral substrates) strongly favors the (R)-isomer of I that demonstrates for the first time that the enzyme has hidden potency for stereospecificity.
 IT 137945-92-7P
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological

activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and tolerance studies in vivo and in vitro of spermine
derivs.)

RN 137945-92-7 CAPLUS
CN 1,3-Butanediamine, N1-(4-aminobutyl)-, trihydrochloride (9CI) (CA INDEX
NAME)



● 3 HCl

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:149929 CAPLUS

DOCUMENT NUMBER: 142:385921

TITLE: Metabolic Stability of α -Methylated Polyamine
Derivatives and Their Use as Substitutes for the
Natural Polyamines

AUTHOR(S): Jaervinen, Aki; Grigorenko, Nikolay; Khomutov, Alex
R.; Hyvoenen, Mervi T.; Uimari, Anne; Vepsaelaeinen,
Jouko; Sinervirta, Riitta; Keinaenen, Tuomo A.;
Vujcic, Slavoljub; Alhonen, Leena; Porter, Carl W.;
Jaenne, Juhani

CORPORATE SOURCE: A. I. Virtanen Institute for Molecular Sciences,
University of Kuopio, Kuopio, FIN-70211, Finland

SOURCE: Journal of Biological Chemistry (2005), 280(8),
6595-6601

PUBLISHER: CODEN: JBCHA3; ISSN: 0021-9258
American Society for Biochemistry and Molecular
Biology

DOCUMENT TYPE: Journal
LANGUAGE: English

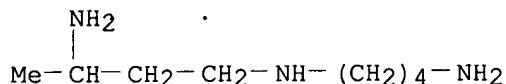
AB Metabolically stable polyamine derivs. may serve as useful surrogates for the natural polyamines in studies aimed to elucidate the functions of individual polyamines. Here we studied the metabolic stability of α -methylspermidine, α -methylspermine, and bis- α -methylspermine, which all have been reported to fulfill many of the putative physiol. functions of the natural polyamines. In vivo studies were performed with the transgenic rats overexpressing spermidine/spermine N1-acetyltransferase. α -Methylspermidine effectively accumulated in the liver and did not appear to undergo any further metabolism. On the other hand, α -methylspermine was readily converted to α -methylspermidine and spermidine; similarly, bis- α -methylspermine was converted to α -methylspermidine to some extent, both conversions being inhibited by the polyamine oxidase inhibitor N1,N2-bis(2,3-butadienyl)-1,4-butanediamine. Furthermore, we used recombinant polyamine oxidase, spermidine/spermine N1-acetyltransferase, and the recently discovered spermine oxidase in the kinetic studies. In vitro studies confirmed that methylation did not protect spermine analogs from degradation, whereas the spermidine analog was stable. Both α -methylspermidine and bis- α -methylspermine overcame the proliferative block of early liver regeneration in transgenic rats and reversed the cytostasis induced by an inhibition of ornithine decarboxylase in cultured fetal fibroblasts.

IT 150333-68-9

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolic stability of α -methylated polyamine derivs. and their
use as substitutes for natural polyamines)

RN 150333-68-9 CAPLUS

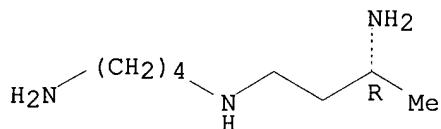
CN 1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:688737 CAPLUS
 DOCUMENT NUMBER: 144:274446
 TITLE: Synthesis of (R)- and (S)-isomers of
 1-methylspermidine
 AUTHOR(S): Grigorenko, Nikolay A.; Vepsalainen, Jouko; Jarvinen,
 Aki; Keinanen, Tuomo; Alhonen, Leena; Janne, Juhani;
 Khomutov, Alex R.
 CORPORATE SOURCE: V.A. Engelhardt Institute of Molecular Biology,
 Russian Academy of Sciences, Moscow, 119991, Russia
 SOURCE: Mendeleev Communications (2005), (4), 142-143
 CODEN: MENCEX; ISSN: 0959-9436
 PUBLISHER: Russian Academy of Sciences
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Previously unknown (R)- and (S)-isomers of 1,8-diamino-5-azanonane were
 prepared starting from (R)- and (S)-2-aminopropanols.
 IT 878133-12-1P 878133-13-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (synthesis of (R)- and (S)-isomers of 1-methylspermidine)
 RN 878133-12-1 CAPLUS
 CN 1,3-Butanediamine, N1-(4-aminobutyl)-, trihydrochloride, (3R)- (9CI) (CA
 INDEX NAME)

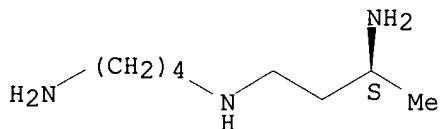
Absolute stereochemistry. Rotation (+).



• 3 HCl

RN 878133-13-2 CAPLUS
CN 1,3-Butanediamine, N1-(4-aminobutyl)-, trihydrochloride, (3S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (-).



● 3 HCl

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:552063 CAPLUS
DOCUMENT NUMBER: 141:82364

TITLE: Spermidine analogs for prevention and treatment of pancreatitis and induction of liver regeneration
 INVENTOR(S): Rasanen, Tiina-Liisa; Alhonen, Leena; Sinervirta, Riitta; Keinanen, Tuomo; Herzog, Karl-Heinz; Khomutov, Alex Radii; Vepsalainen, Jouko; Janne, Juhani
 PATENT ASSIGNEE(S): Tiina-Liisa Rasanen, Finland; Leena Alhonen; Riitta Sinervirta; Tuomo Keinanen; Karl-Heinz Herzog; Alex Radii Khomutov; Jouko Vepsalainen; Juhani Janne
 SOURCE: Jpn. Kokai Tokkyo Koho, 51 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

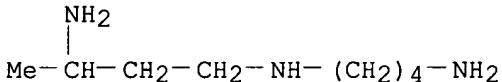
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004189714	A2	20040708	JP 2003-33882	20030212
CA 2413720	AA	20040609	CA 2002-2413720	20021209
CA 2452467	AA	20040609	CA 2003-2452467	20031209
US 2004180968	A1	20040916	US 2003-731626	20031209
PRIORITY APPLN. INFO.:			US 2002-431958P	P 20021209
			CA 2002-2413720	A 20021209

OTHER SOURCE(S): MARPAT 141:82364
 AB Spermidine analogs (I; R₂R₁N(CR₃R₄)aN(R₁₀)(CR₅R₆)bN(R₁₁)[(CR₇R₈)cN(R₁₂)]nR
 9 wherein a, b, c = 1-6; n = 0, 1; R₁-R₁₂ = H, alkyl), including
 1-methylspermidine, are claimed for prevention and treatment of
 pancreatitis and induction of liver regeneration.

IT 150333-68-9
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (spermidine analogs for prevention and treatment of pancreatitis and
 induction of liver regeneration)

RN 150333-68-9 CAPLUS

CN 1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 17 USPATFULL on STN
 ACCESSION NUMBER: 2004:233894 USPATFULL
 TITLE: Methods for the treatment and prevention of
 pancreatitis and for induction of liver regeneration
 INVENTOR(S): Rasanen, Tiina-Liisa, Syvanniemi, FINLAND
 Alhonen, Leena, Vuorela, FINLAND
 Sinervirta, Riitta, Syvanniemi, FINLAND
 Keinanen, Tuomo, Kuopio, FINLAND
 Herzog, Karl-Heinz, Kuopio, FINLAND
 Khomutov, Alex Radii, Moscow, RUSSIAN FEDERATION
 Vepsalainen, Jouko, Kuopio, FINLAND
 Janne, Juhani, Vuorela, FINLAND

PATENT INFORMATION:	NUMBER	KIND	DATE
APPLICATION INFO.:	US 2004180968	A1	20040916
	US 2003-731626	A1	20031209 (10)

PRIORITY INFORMATION:	NUMBER	DATE
DOCUMENT TYPE:	US 2002-431958P	20021209 (60)
FILE SEGMENT:	Utility	
LEGAL REPRESENTATIVE:	WOODCOCK WASHBURN LLP, ONE LIBERTY PLACE, 46TH FLOOR, 1650 MARKET STREET, PHILADELPHIA, PA, 19103	
NUMBER OF CLAIMS:	30	

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 2039

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel methods for treating and preventing acute and/or chronic pancreatitis are described. Additionally, novel methods for inducing liver regeneration are described. The methods may comprise administering to a patient an effective amount of a metabolically stable analogue of spermidine and/or spermine. Preferred compounds for use in the methods may include 1-methylspermidine, 1-methylspermine and 1,12-dimethylspermine.

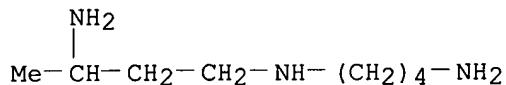
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 150333-68-9

(spermidine analogs for prevention and treatment of pancreatitis and induction of liver regeneration)

RN 150333-68-9 USPATFULL

CN 1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:642169 CAPLUS

DOCUMENT NUMBER: 141:395701

TITLE: A New Synthesis of α -Methylspermidine

AUTHOR(S): Grigorenko, N. A.; Vepsalainen, J.; Jarvinen, A.; Keinanen, T. A.; Alhonen, L.; Janne, J.; Kritsyn, A. M.; Khomutov, A. R.

CORPORATE SOURCE: Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, 119991, Russia

SOURCE: Russian Journal of Bioorganic Chemistry (Translation of Bioorganicheskaya Khimiya) (2004), 30(4), 396-399

CODEN: RJBCET; ISSN: 1068-1620

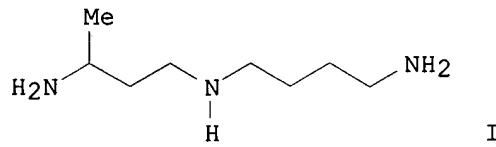
PUBLISHER: MAIK Nauka/Interperiodica Publishing

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:395701

GI



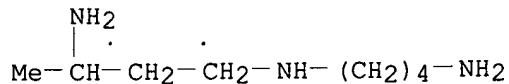
AB A five-step synthesis of α -methylspermidine (1,8-diamino-5-azanonane, I·3 HCl), the first polyamine analog preventing pathol. consequences of spermidine depletion in transgenic rats overproducing spermine/spermidine N1-acetyltransferase (no data), from Et 3-aminobutyrate was achieved in a high overall yield.

IT 137945-92-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(new synthesis of α -methylspermidine)

RN 137945-92-7 CAPLUS

CN 1,3-Butanediamine, N1-(4-aminobutyl)-, trihydrochloride (9CI) (CA INDEX NAME)



● 3 HCl

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 17 USPATFULL on STN
 ACCESSION NUMBER: 2003:207355 USPATFULL
 TITLE: Novel glycosidase inhibitors and their pharmacological uses, in particular for treating diabetes
 INVENTOR(S): Aghajari, Nushin Banu Helene, Lyon, FRANCE
 Robert, Xavier Guy, Lyon, FRANCE
 Haser, Richard Michel, Lyon, FRANCE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003143713	A1	20030731
APPLICATION INFO.:	US 2002-168703	A1	20021024 (10)
	WO 2000-FR3600		20001220

	NUMBER	DATE
PRIORITY INFORMATION:	FR 1999-16409	19991223
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	YOUNG & THOMPSON, 745 SOUTH 23RD STREET 2ND FLOOR, ARLINGTON, VA, 22202	

NUMBER OF CLAIMS: 12
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 6 Drawing Page(s)
 LINE COUNT: 959

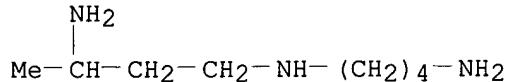
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns the use of a polyamine derivative or a polyamine for inhibiting the active site of glycosidase enzymes intervening in the transformation of polysaccharides into sugars, in particular into glucose, in a living organism.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 150333-68-9D, α -amylase complexes
 (polyamines and polyamine derivs. as glycosidase inhibitors and pharmacol. use, especially for treating diabetes)

RN 150333-68-9 USPATFULL
 CN 1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2001:489237 CAPLUS
 DOCUMENT NUMBER: 135:71297
 TITLE: Polyamines and polyamine derivatives as glycosidase inhibitors and their pharmacological uses, in particular for treating diabetes
 INVENTOR(S): Aghajari, Nushin Banu Helene; Robert, Xavier Guy; Haser, Richard Michel
 PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique, Fr.
 SOURCE: PCT Int. Appl., 46 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY. ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047528	A2	20010705	WO 2000-FR3600	20001220
WO 2001047528	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2802817	A1	20010629	FR 1999-16409	19991223
FR 2802817	B1	20021011		
CA 2395305	AA	20010705	CA 2000-2395305	20001220
EP 1239863	A2	20020918	EP 2000-990069	20001220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518501	T2	20030610	JP 2001-548121	20001220
US 2003143713	A1	20030731	US 2002-168703	20021024
PRIORITY APPLN. INFO.:			FR 1999-16409	A 19991223
			WO 2000-FR3600	W 20001220

OTHER SOURCE(S): MARPAT 135:71297

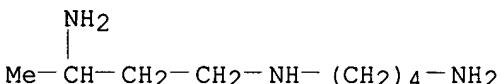
AB The invention discloses the use of a polyamine or polyamine derivative for inhibiting the active site of glycosidases converting polysaccharides into sugars, in particular into glucose, in a living organism. The compds. of the invention are useful in the treatment of diabetes.

IT 150333-68-9D, α -amylase complexes

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(polyamines and polyamine derivs. as glycosidase inhibitors and pharmacol. use, especially for treating diabetes)

RN 150333-68-9 CAPLUS

CN 1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:252763 CAPLUS

DOCUMENT NUMBER: 135:73053

TITLE: Circular Dichroism and NMR Studies of Metabolically Stable α -Methylpolyamines: Spectral Comparison with Naturally Occurring Polyamines

AUTHOR(S): Varnado, Byron L.; Voci, Christopher J.; Meyer, Lynn M.; Coward, James K.

CORPORATE SOURCE: Departments of Medicinal Chemistry and Chemistry, The University of Michigan, Ann Arbor, MI, 48109-1055, USA

SOURCE: Bioorganic Chemistry (2000), 28(6), 395-408
CODEN: BOCMBM; ISSN: 0045-2068

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Three synthetic polyamine analogs, α -methylspermidine, α -methylspermine, and α, α' -dimethylspermine, were compared with their naturally occurring counterparts, spermidine and spermine, by two different spectral techniques. The interaction of polyamines with oligodeoxynucleotides was measured by CD in order to monitor the polyamine-induced conversion of right-handed B-DNA to the left-handed Z-form. The methylated analogs were shown to be equally

effective as the natural polyamines in inducing the B \rightarrow Z transition. The pH dependence of the chemical shift of all carbon atoms in each of the five polyamines was measured by ^{13}C -NMR spectroscopy. With the exception of expected changes in chemical shift due to the presence of the α -Me substituents, the chemical shifts and pH dependence of all carbon atoms in the three α -Me polyamines were similar to the corresponding naturally occurring polyamines. The combined data indicate that α -Me polyamines have phys. properties that are very similar to their natural counterparts. The two metabolically stable polyamine analogs, α -methylspermidine and α, α' -dimethylspermine, are therefore useful surrogates for spermidine and spermine in the study of numerous polyamine-mediated effects in mammalian cell cultures and can be used in such studies without the requirement for coadministration of amine oxidase inhibitors. (c) 2000 Academic Press.

IT

150333-68-9

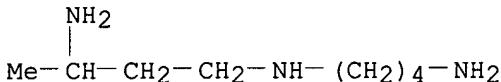
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(metabolically stable Me polyamine analogs have phys. properties that are very similar to their natural counterparts)

RN

150333-68-9 CAPLUS

CN

1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

27

THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1994:570535 CAPLUS
 DOCUMENT NUMBER: 121:170535
 TITLE: Compositions and methods for inhibiting deoxyhypusine synthase and the growth of cells
 INVENTOR(S): Jakus, Judit; Park, Myung Hee; Wolff, Edith C.; Folk, John E.
 PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
 SOURCE: PCT Int. Appl., 50 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9415596	A1	19940721	WO 1993-US12310	19931216
W: AU, CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5344846	A	19940906	US 1992-998231	19921230
AU 9458722	A1	19940815	AU 1994-58722	19931216
PRIORITY APPLN. INFO.:			US 1992-998231	A 19921230
			WO 1993-US12310	W 19931216

OTHER SOURCE(S): MARPAT 121:170535

AB Compns. and methods for the treatment of mammalian cells to inhibit cell growth, especially for inhibiting the proliferative cell growth associated with malignant and non-malignant disease, are provided. More particularly, a deoxyhypusine synthase inhibitor, typically, a mono- or bisguanyl diamine or polyamine, is administered to the cells. Also provided by this invention are diagnostic methods and kits for screening the cells of a patient to determine the effect of the deoxyhypusine synthase inhibitor on proliferation of the cells. Synthesis of compds. is given as is assay of enzyme inhibitory activity. Structure effects on activity is discussed.

IT

150333-68-9

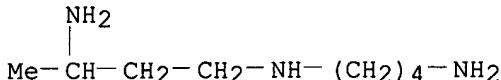
RL: PRP (Properties)

(activity of, against deoxyhypusine synthase of rat testis)

RN

150333-68-9 CAPLUS

CN 1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 12 OF 17 USPATFULL on STN

ACCESSION NUMBER:

94:77732 USPATFULL

TITLE:

Compositions and methods for inhibiting deoxyhypusine synthase and the growth of cells

INVENTOR(S):

Jakus, Judit, Silver Spring, MD, United States

Park, Myung H., Potomac, MD, United States

Wolff, Edith C., Bethesda, MD, United States

Folk, John E., Derwood, MD, United States

PATENT ASSIGNEE(S):

The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5344846		19940906
APPLICATION INFO.:	US 1992-998231		19921230 (7)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	O'Sullivan, Peter		
LEGAL REPRESENTATIVE:	Townsend and Townsend Khourie and Crew		
NUMBER OF CLAIMS:	5		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 6 Drawing Page(s)		
LINE COUNT:	1121		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compositions and methods for the treatment of mammalian cells to inhibit cell growth, especially for inhibiting the proliferative cell growth associated with malignant and non-malignant disease, are provided. More particularly, a deoxyhypusine synthase inhibitor, typically, a mono- or bisguanyl diamine or polyamine, is administered to the cells.

Also provided by this invention are diagnostic methods and kits for screening the cells of a patient to determine the effect of the deoxyhypusine synthase inhibitor on proliferation of the cells.

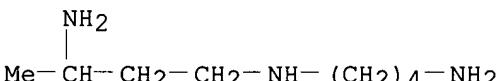
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 150333-68-9

(activity of, against deoxyhypusine synthase of rat testis)

RN 150333-68-9 USPATFULL

CN 1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:627393 CAPLUS

DOCUMENT NUMBER: 121:227393

TITLE: The role of hypusine depletion in cytostasis induced by S-adenosyl-L-methionine decarboxylase inhibition: new evidence provided by 1-methylspermidine and 1,12-dimethylspermine

AUTHOR(S): Byers, Timothy L.; Lakanen, John R.; Coward, James K.; Pegg, Anthony E.

CORPORATE SOURCE: Department of Cell and Molecular Physiology, M.S. Hershey Medical Center, Hershey, PA, 17033, USA

SOURCE: Biochemical Journal (1994), 303(2), 363-8

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The abilities of the natural polyamines, spermidine and spermine, and of the synthetic analogs, 1-methylspermidine and 1,12-dimethylspermine, to reverse the effects of the S-adenosyl-L-methionine decarboxylase inhibitor 5'-{[(Z)-4-aminobut-2-enyl]methylamino}-5'-deoxyadenosine (AbeAdo) on L1210-cell growth were studied. L1210 cells were exposed to AbeAdo for 12 days to induce cytostasis and then exposed to spermidine, spermine, 1-methylspermidine or 1,12-dimethylspermine in the continued presence of AbeAdo. AbeAdo-induced cytostasis was overcome by the natural polyamines, spermidine and spermine. The cytostasis was also reversed by 1-methylspermidine. 1,12-Dimethylspermine had no effect on the AbeAdo-induced cytostasis of chronically treated cells, although it was active in permitting growth of cells treated with the ornithine decarboxylase inhibitor, α -difluoromethylornithine. The initial 12-day exposure to AbeAdo elevated intracellular putrescine levels, depleted intracellular spermidine and spermine, and resulted in the accumulation of unmodified eukaryotic translation initiation factor 5A (eIF-5A). Exposure of these cells to exogenous spermidine, which is the natural substrate for deoxyhypusine synthase, resulted in a decrease in the unmodified eIF-5A content. 1-Methylspermidine, which was found to be a substrate of deoxyhypusine synthase in vitro, also decreased the levels of unmodified eIF-5A in the AbeAdo-treated cells. Although spermine is not a substrate of deoxyhypusine synthase, spermine was converted into spermidine in the L1210 cells, and spermine addition to AbeAdo-treated cells resulted in the appearance of both intracellular spermine and spermidine and in the decrease in unmodified eIF-5A. Exogenous 1,12-dimethylspermine, which was not metabolized to spermine or to 1-methylspermidine and was not a substrate of deoxyhypusine synthase in vitro, did not decrease levels of unmodified eIF-5A. The finding that AbeAdo-induced cytostasis was only reversed by polyamines and polyamine analogs that result in the formation of hypusine or an analog in eIF-5A is consistent with the hypothesis (Byers, T. L., 1993) that AbeAdo-induced cytostasis is due to the depletion of the hypusine-containing form of eIF-5A, which is secondary to the depletion of spermidine by inhibition of S-adenosyl-L-methionine decarboxylase.

IT

150333-68-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

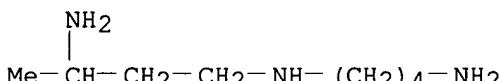
(evidence provided by 1-methylspermidine and 1,12-dimethylspermine for the role of hypusine depletion in cytostasis induced by S-adenosyl-L-methionine decarboxylase inhibition)

RN

150333-68-9 CAPLUS

CN

1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:576449 CAPLUS

DOCUMENT NUMBER: 119:176449

TITLE: Features of the spermidine-binding site of deoxyhypusine synthase as derived from inhibition studies. Effective inhibition by bis- and mono-guanylated diamines and polyamines

AUTHOR(S): Jakus, Judit; Wolff, Edith C.; Park, Myung Hee; Folk, J. E.

CORPORATE SOURCE: Lab. Cell. Dev. Oncol., Natl. Inst. Dent. Res., Bethesda, MD, 20892, USA

SOURCE: Journal of Biological Chemistry (1993), 268(18), 13151-9

DOCUMENT TYPE: CODEN: JBCHA3; ISSN: 0021-9258

LANGUAGE: Journal

LANGUAGE: English

AB Several types of basic compds. structurally related to spermidine, one of the substrates for deoxyhypusine synthase, were tested as inhibitors of this enzyme. The results indicate that inhibitory compds. associate with the enzyme at the site of spermidine binding and must possess two charged primary amino or guanidino groups, or one of each. The efficiency of inhibition is related to the maximum possible distance between the primary amino groups and is adversely affected by substitutions on the secondary amino group or in the carbon chains of polyamines. The mono-guanyl derivs. are much more effective inhibitors than the parent amines or their bis-guanylated counterparts, N1-guanyl-1,7-diaminoheptane being the most effective compound with a Ki value of about 10 nM. Based on these observations a model is proposed for the spermidine-binding site of deoxyhypusine synthase. Studies with Chinese hamster ovary cells reveal a direct correlation between prevention of hypusine formation by several guanyldiamines and their in vitro inhibition of deoxyhypusine synthase. This evidence for disruption of the initial step in the post-translational maturation of eukaryotic initiation factor 5A provides a basis for the potential control of protein biosynthesis and cell proliferation.

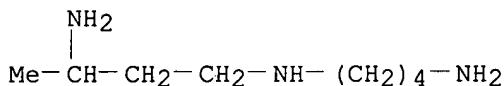
IT 150333-68-9

RL: BIOL (Biological study)

(deoxyhypusine synthase inhibition by, structure relation to)

RN 150333-68-9 CAPLUS

CN 1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:105949 CAPLUS

DOCUMENT NUMBER: 116:105949

TITLE: α -Methyl polyamines: metabolically stable spermidine and spermine mimics capable of supporting growth in cells depleted of polyamines

AUTHOR(S): Lakanen, John R.; Coward, James K.; Pegg, Anthony E.

CORPORATE SOURCE: Dep. Chem., Univ. Michigan, Ann Arbor, MI, 48109-1055, USA

SOURCE: Journal of Medicinal Chemistry (1992), 35(4), 724-34

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In order to assess the tolerance of the target enzyme spermine synthase for α -substituents on the aminopropyl moiety of the substrate spermidine, 1-methylspermidine (I) was synthesized. I is a poor substrate for spermine synthase and is not a substrate for spermidine N1-acetyltransferase, suggesting that α -methylated polyamines might be metabolically stable and therefore useful tools for studying polyamine effects in intact cells. On the basis of initial cellular results with I, 1-methylspermine (II) and 1,12-dimethylspermine (III) were also synthesized. When added to cells (L1210, SV-3T3, or HT29) depleted of both putrescine and spermidine by prior treatment with α -(difluoromethyl)ornithine (IV), these α -methylated polyamines were able to restore cell growth to that observed in the absence of IV. In accord with the enzyme data noted above, metabolic studies indicated a slow conversion of I to II, but no metabolism of III in these cells. It was concluded from these results that the α -methylated polyamines are able to substitute for the natural polyamines, spermidine and spermine in critical biochem. processes which involve polyamines for continued cell growth. In accord with the hypothesis, preliminary data indicate that I and III are as effective as spermidine and spermine, resp., in promoting the conversion of B-DNA to Z-DNA.

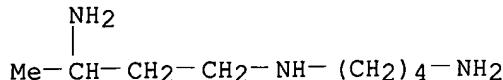
IT 137945-92-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 137945-92-7 CAPLUS

CN 1,3-Butanediamine, N1-(4-aminobutyl)-, trihydrochloride (9CI) (CA INDEX)

NAME)



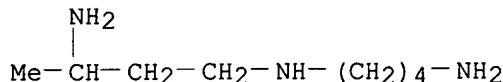
● 3 HCl

IT 150333-68-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as spermidine acetyltransferase substrate)

RN 150333-68-9 CAPLUS

CN 1,3-Butanediamine, N1-(4-aminobutyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1980:441626 CAPLUS

DOCUMENT NUMBER: 93:41626

TITLE: Coexistence of two pathways of spermidine biosynthesis
in *Lathyrus sativus* seedlings

AUTHOR(S): Srivenugopal, K. S.; Adiga, P. R.

CORPORATE SOURCE: Biochem. Dep., Indian Inst. Sci., Bangalore, 560012,
India

SOURCE: FEBS Letters (1980), 112(2), 260-4
CODEN: FEBLAL; ISSN: 0014-5793

DOCUMENT TYPE: Journal

LANGUAGE: English

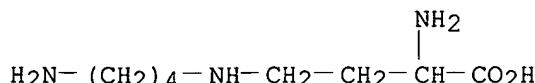
AB Evidence for the coexistence of both the classical S-adenosyl-L-methionine
decarboxylase pathway and a recently proposed new route (aspartic
β-semialdehyde forms a Schiff base with putrescine to be enzymically
reduced by an NADPH-dependent step to yield "carboxyspermidine", which in
turn undergoes a pyridoxal phosphate-dependent enzymic decarboxylation to
give rise to spermidine) of spermidine biosynthesis in *L. sativus*
seedlings is presented. The latter biosynthetic sequence is primarily
restricted to spermidine synthesis.

IT 61715-48-8

RL: BIOL (Biological study)
(as intermediate in spermidine biosynthetic pathway in *Lathyrus*
sativus)

RN 61715-48-8 CAPLUS

CN Butanoic acid, 2-amino-4-[(4-aminobutyl)amino]- (9CI) (CA INDEX NAME)



L4 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1977:52515 CAPLUS

DOCUMENT NUMBER: 86:52515

TITLE: A new pathway for the biosynthesis of spermidine
Tait, George H.

AUTHOR(S): Med. Sch., St. Mary's Hosp., London, UK

CORPORATE SOURCE: Biochemical Society Transactions (1976), 4(4), 610-12
SOURCE: CODEN: BCSTB5; ISSN: 0300-5127

DOCUMENT TYPE: Journal

LANGUAGE: English

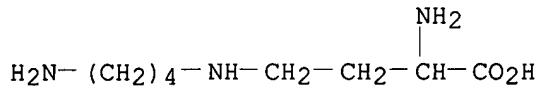
AB Studies of spermidine formation in *Micrococcus denitrificans* and *Rhodopseudomonas sphaeroides* using labeled precursors indicated the presence of an intermediate carboxyspermidine, $\text{H}_2\text{N}(\text{CH}_2)_4\text{NH}(\text{CH}_2)_2\text{CH}(\text{NH}_2)\text{CO}_2\text{H}$ (I), formed by reduction of a Schiff's base. In the presence of pyridoxal phosphate, I was decarboxylated to spermidine.

IT 61715-48-8

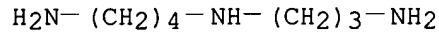
RL: BIOL (Biological study)
(in spermidine formation, in *Micrococcus denitrificans* and
Rhodopseudomonas sphaeroides)

RN 61715-48-8 CAPLUS

CN Butanoic acid, 2-amino-4-[(4-aminobutyl)amino]- (9CI) (CA INDEX NAME)



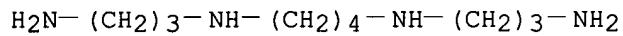
L7 ANSWER 3270 OF 3272 REGISTRY COPYRIGHT 2006 ACS on STN
RN 124-20-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN 1,4-Butanediamine, N-(3-aminopropyl)- (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spermidine (6CI)
OTHER NAMES:
CN 1,5,10-Triazadecane
CN 1,8-Diamino-4-azaoctane
CN 4-Azaoctane-1,8-diamine
CN N-(3-Aminopropyl)-1,4-butanediamine
CN N-(3-Aminopropyl)-1,4-diaminobutane
CN N-(3-Aminopropyl)-4-aminobutylamine
CN N-(4-Aminobutyl)-1,3-diaminopropane
CN Spermidin
FS 3D CONCORD
MF C7 H19 N3
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA,
CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM,
DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA,
MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PIRA, PROMT, RTECS*, SPECINFO,
SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9434 REFERENCES IN FILE CA (1907 TO DATE)
284 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9446 REFERENCES IN FILE CAPLUS (1907 TO DATE)
86 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L8 ANSWER 402 OF 402 REGISTRY COPYRIGHT 2006 ACS on STN
RN 71-44-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN 1,4-Butanediamine, N,N'-bis(3-aminopropyl)- (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Spermine (6CI)**
OTHER NAMES:
CN 1,5,10,14-Tetraazatetradecane
CN 4,9-Diazadodecane-1,12-diamine
CN Gerontine
CN Musculamine
CN N,N'-Bis(3-aminopropyl)-1,4-butanediamine
CN N,N'-Bis(3-aminopropyl)-1,4-tetramethylenediamine
CN Neuridine
CN NSC 268508
CN Spermin
FS 3D CONCORD
DR 115-04-8
MF C10 H26 N4
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*,
BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS,
CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGU,
EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS,
NAPRALERT, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USPAT2,
USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9218 REFERENCES IN FILE CA (1907 TO DATE)
319 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9230 REFERENCES IN FILE CAPLUS (1907 TO DATE)
106 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

ACCESSION NUMBER: 81002150 EMBASE

DOCUMENT NUMBER: 1981002150

TITLE: The role of phospholipase A in acute **pancreatitis**

AUTHOR: Nevalainen T.J.

CORPORATE SOURCE: Lab. Electron Microscopy, Univ. Turku, 20520 Turku 52, Finland

SOURCE: Scandinavian Journal of Gastroenterology, (1980) Vol. 15, No. 6, pp. 641-650. .

CODEN: SJGRA4

COUNTRY: Norway

DOCUMENT TYPE: Journal

FILE SEGMENT: 048 Gastroenterology

029 Clinical Biochemistry

LANGUAGE: English

ENTRY DATE: Entered STN: 9 Dec 1991

Last Updated on STN: 9 Dec 1991

AB Phospholipase A is a hydrolytic enzyme that splits one fatty acid off the phospholipid, e.g. from lecithin to form lysolecithin. Calcium ions and bile salt are essential for the enzymatic activity. The enzyme is synthesized by the pancreatic acinar cells, liberated to the pancreatic juice, and secreted in the duodenum for digestive purposes. It is synthesized and secreted under normal circumstances in enzymatically inactive as prophospholipase A, which is activated for trypsin.

Phospholipase A is inhibited by e.g. zinc, EDTA, haloketones, structural analogs of the substrate, polyphloretin phosphate, antimalarial drugs of the chloroquine type, polyamines such as **spermine**,

spermidine, and putrescine, local anesthetics related to procaine including chlorpromazine, and antibiotics including tetracycline and chloramphenicol. The pathogenetic role of phospholipase A in acute **pancreatitis** is supported by the observations that it and lysolecithin, when injected into the pancreatic duct of experimental animals, cause histologically similar changes - namely coagulation necrosis - in the gland as seen in cases of human acute **pancreatitis**. Increased phospholipase A and lysolecithin contents are found in pancreatic tissue in acute **pancreatitis**.

Phospholipase A is elevated in the serum of patients with acute **pancreatitis**. Phospholipase A injected intravenously into experimental animals causes a decrease in arterial blood pressure. The respiratory distress syndrome associated with acute **pancreatitis** can be explained by the action of phospholipase A on the pulmonary surfactant, which consists of phospholipids. The enzyme may also be involved in the development of cerebral demyelination in acute **pancreatitis** and in the formation in ischemic pancreas of a myocardial depressant factor that plays an important role in various forms of circulatory shock. Specific therapy directed to the inhibition of phospholipase A in human and experimental acute **pancreatitis** has been successful with phospholipase A inhibitors such as cytidine diphosphate choline, CaNa2-EDTA, xylocaine, procaine, and chlorpromazine. It is proposed in this review that inhibition and elimination of phospholipase A by enzyme inhibitors and immunochemical means and through detoxication methods such as hemodialysis and hemoperfusion should be investigated to find a novel and effectual treatment for acute **pancreatitis**.

ACCESSION NUMBER: 2006:211169 BIOSIS

DOCUMENT NUMBER: PREV200600212898

TITLE: Trypsin activation is followed by pancreatic polyamine depletion in severe sublethal acute **pancreatitis** model.

AUTHOR(S): Jin, Hailao; Lamsa, Teemu; Sand, Juhani; Ratty, Sari; Herzig, Karl-Heinz; Alhonen, Leena; Nordback, Isto

SOURCE: Gastroenterology, (APR 2005) Vol. 128, No. 4, Suppl. 2, pp. A791.

Meeting Info.: Annual Meeting of the American-Gastroenterological-Association/Digestive-Disease-Week. Chicago, IL, USA. May 14 -19, 2005. Amer Gastroenterol Assoc.

CODEN: GASTAB. ISSN: 0016-5085.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 29 Mar 2006

Last Updated on STN: 29 Mar 2006

AB Background: Previous findings have demonstrated that activation of polyamine catabolism in transgenic rats (over-expressing **spermidine/spermine** N'-acetyltransferase, SSAT) results in acute pancreatic inflammation, suggesting that depletion of polyamines (**spermine** and **spermidine**) may be one step in the evolution of acute **pancreatitis**. The purpose of this study was to explore this hypothesis in another model, and to study the timing of the changes in the polyamine metabolism in relation to trypsin activation.

Methods: 36 rats (300g-350g) were divided into 2 groups (**pancreatitis** group and sham group). In **pancreatitis** group 0.2 ml of 2.0% sodium taurodeoxycholate was infused into the pancreatic duct. In sham group the animals underwent laparotomy only. All animals were sacrificed and sampled under anesthesia at 3h, 24h and 48h. 6 rats served as 0 hour controls without operation. Serum amylase and pancreatic SSAT activities were measured. Pancreatic histology, water content and concentrations of **spermine**, **spermidine** and trypsin activation peptide (TAP) were analysed, Results: In the **pancreatitis** group with hyperamylasemia, pancreatic edema, and **pancreatitis** histology SSAT was induced early, in association with trypsin, resulting in substantial decrease of both **spermine** and **spermidine** (Table). Pancreatic SSAT activity and TAP content correlated with each other (correlation coefficient 0.782, P < 0.05), [GRAPHICS]Conclusions: Another **pancreatitis** model (sodium taurocholate **pancreatitis**) is associated with the depletion of polyamines after induction of SSAT that occurs in association with the trypsin activation. Because polyamine depletion occurs between 3 and 24 h after induction of **pancreatitis**, it may serve as a target for therapy in **pancreatitis**.

L20 ANSWER 8 OF 225 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:613176 CAPLUS
DOCUMENT NUMBER: 89:213176
TITLE: Polyamine metabolism in ethionine-induced rat
pancreatitis
AUTHOR(S): Yoshikawa, Daisuke
CORPORATE SOURCE: Dep. Intern. Med., Kobe Univ. Sch. Med., Kobe, Japan
SOURCE: Kobe Ika Daigaku Kiyo (1978), 37(4), 261-9
CODEN: KIDKA9; ISSN: 0375-927X
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Changes in concentration of putrescine, **spermidine**, and
spermamine and in activity of ornithine decarboxylase were examined in
pancreas of rat in which **pancreatitis** was induced by i.p.
injection of ethionine in addition to protein deprivation from food for 5
days. Ornithine decarboxylase activity decreased to about 1/10 of
preinjection value of 1st day of ethionine administration. Putrescine
concentration increased continuously during ethionine injection, whereas
spermidine and **spermamine** decreased slowly to about 1/2 of
preinjection value. After treatment for 5 days, ethionine administration
was discontinued and a normal diet was given. Ornithine decarboxylase
activity increased to 39-times of preinjection value 3.5 days after the
discontinuation of the treatment, followed by a rapid decrease.
Putrescine concentration decreased immediately after the discontinuation, whereas
spermidine and **spermamine** increased continuously and
reached preinjection levels 10 days after discontinuation.

ACCESSION NUMBER: 2002:783211 CAPLUS

DOCUMENT NUMBER: 138:331376

TITLE: A Polyamine Analogue Prevents Acute
Pancreatitis and Restores Early Liver
Regeneration in Transgenic Rats with Activated
Polyamine CatabolismAUTHOR(S): Raesaenen, Tiina-Liisa; Alhonen, Leena; Sinervirta,
Riitta; Keinaenen, Tuomo; Herzig, Karl-Heinz; Suppola,
Suvikki; Khomutov, Alex R.; Vepsaelaeinen, Jouko;
Jaenne, JuhaniCORPORATE SOURCE: A.I. Virtanen Institute for Molecular Sciences,
University of Kuopio, Kuopio, FIN-70211, FinlandSOURCE: Journal of Biological Chemistry (2002), 277(42),
39867-39872

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We recently generated a transgenic rat model for acute **pancreatitis**, which was apparently caused by a massive depletion of pancreatic polyamines **spermidine** and **spermine** due to inducible activation of their catabolism (Alhonen, L., Parkkinen, J. J., Keinaenen, T., Sinervirta, R., Herzig, K. H., and Jaenne, J. (2000) Proc. Natl. Acad. Sci. U. S. A. 97, 8290-8295). When subjected to partial hepatectomy, these animals showed striking activation of polyamine catabolism at 24 h postoperatively with a profound decrease in hepatic **spermidine** and **spermine** pools and failure to initiate liver regeneration. Here we show that **pancreatitis** in this model could be totally prevented, as judged by histopathol. and plasma α -amylase activity, by administration of 1-methylspermidine, a metabolically stable analog of **spermidine**. Similarly, the analog, given prior to partial hepatectomy, restored early liver regeneration in the transgenic rats, as indicated by a dramatic increase in the number of proliferating cell nuclear antigen-pos. hepatocytes from about 1% to more than 40% in response to the drug. The present results suggest that the extremely high concentration of **spermidine** in the pancreas, in fact the highest in the mammalian body, may have a critical role in maintaining organ integrity. The failure to initiate liver regeneration in the absence of sufficient hepatic polyamine pools similarly indicates that polyamines are required for proper commencement of the regenerative process.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'HOME' ENTERED AT 16:51:57 ON 12 JUN 2006)

FILE 'REGISTRY' ENTERED AT 16:56:36 ON 12 JUN 2006
STRUCTURE uploaded
7 S SSS L1 FULL

FILE 'CAPLUS, BIOSIS, EMBASE, USPATFULL' ENTERED AT 16:57:07 ON 12 JUN 2006

L3 17 S L2
L4 17 DUP REM L3 (0 DUPLICATES REMOVED)

FILE 'REGISTRY' ENTERED AT 16:58:57 ON 12 JUN 2006
402 S SPERIDINE OR SPERMINE
3538 S SPERMIDINE OR SPERMINE
3272 S SPERMIDINE
402 S SPERMINE

FILE 'CAPLUS, BIOSIS, EMBASE, USPATFULL' ENTERED AT 17:00:30 ON 12 JUN 2006

L9 45511 S SPERMINE OR SPERMIDINE
L10 46273 S L9 OR 71-44-3/RN OR 124-20-9/RN
L11 46273 S L10
L12 342976 S PANCREATITIS OR PANCREASE OR GREY TURNER SIGN OR CHOLELITHIAS
L13 1712 S L11 AND L12
L14 1684 S L11 AND (PANCREATITIS OR PANCREATIC OR GREY TURNER SIGN)
L15 1678 S L14 AND (SPERMIDINE OR SPERMIN OR SPERMINE)
L16 1358 S L14 AND (SPERMIDINE)
L17 1358 FOCUS L16 1-

=> s 111 and (pancreatitis or pancrease inflammation)
L18 236 L11 AND (PANCREATITIS OR PANCREASE INFLAMMATION)

```
=> dup rem l18
PROCESSING COMPLETED FOR L18
L19          225 DUP REM L18 (11 DUPLICATES REMOVED)
```

=> focus
PROCESSING COMPLETED FOR L19
L20 225 FOCUS L19 1-

=> s 111 and (pancreatitis)
L21 236 L11 AND (PANCREATITIS)

=> d ibib abs 1-30 120

L20 ANSWER 1 OF 225 USPATFULL on STN
ACCESSION NUMBER: 2004:233894 USPATFULL
TITLE: Methods for the treatment and prevention of
pancreatitis and for induction of liver
regeneration
INVENTOR(S): Rasanen, Tiina-Liisa, Syvanniemi, FINLAND
Alhonen, Leena, Vuorela, FINLAND
Sinervirta, Riitta, Syvanniemi, FINLAND
Keinanen, Tuomo, Kuopio, FINLAND
Herzig, Karl-Heinz, Kuopio, FINLAND
Khomutov, Alex Radii, Moscow, RUSSIAN FEDERATION
Vepsalainen, Jouko, Kuopio, FINLAND
Janne, Juhani, Vuorela, FINLAND

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004180968	A1	20040916
APPLICATION INFO:	US 2003-731626	A1	20031209 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-431958P	20021209 (60)
DOCUMENT TYPE:	Utility	

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WOODCOCK WASHBURN LLP, ONE LIBERTY PLACE, 46TH FLOOR,
NUMBER OF CLAIMS: 1650 MARKET STREET, PHILADELPHIA, PA, 19103
EXEMPLARY CLAIM: 30
NUMBER OF DRAWINGS: 1
LINE COUNT: 10 Drawing Page(s)
2039
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel methods for treating and preventing acute and/or chronic **pancreatitis** are described. Additionally, novel methods for inducing liver regeneration are described. The methods may comprise administering to a patient an effective amount of a metabolically stable analogue of **spermidine** and/or **spermine**. Preferred compounds for use in the methods may include 1-methylspermidine, 1-methylspermine and 1,12-dimethylspermine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L20 ANSWER 2 OF 225 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:195392 CAPLUS
DOCUMENT NUMBER: 143:303698
TITLE: Acute **pancreatitis** induced by activation of the polyamine catabolism in gene-modified mice and rats overexpressing **spermidine**/**spermine** N1-acetyltransferase
AUTHOR(S): Herzog, Karl-Heinz; Janne, Juhani; Alhonen, Leena
CORPORATE SOURCE: Department of Biotechnology and Molecular Medicine, A.I. Virtanen Institute for Molecular Sciences, University of Kuopio, Finland
SOURCE: Scandinavian Journal of Gastroenterology (2005), 40(1), 120-121
CODEN: SJGRA4; ISSN: 0036-5521
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Premature intracellular activation of digestive zymogens is the initiating factor in the course of acute **pancreatitis**. In transgenic rats overexpressing **spermidine**/**spermine** N1-acetyltransferase (SSAT) gene under the control of an inducible mouse metallothionein I promoter, administration of zinc resulted in acute **pancreatitis** by depletion of **spermidine** and **spermine**. A sufficient pool of higher polyamine levels seems therefore essential to maintain pancreatic integrity. The induction of **pancreatitis** by activation of SSAT could be prevented by the administration of 1-methylspermidine, a metabolically stable analog of **spermidine**.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 225 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:525360 CAPLUS
DOCUMENT NUMBER: 133:221079
TITLE: Activation of polyamine catabolism in transgenic rats induces acute **pancreatitis**
AUTHOR(S): Alhonen, Leena; Parkkinen, Jyrki J.; Keinanen, Tuomo; Sinervoita, Riitta; Herzog, Karl-Heinz; Janne, Juhani
CORPORATE SOURCE: A. I. Virtanen Institute for Molecular Sciences, University of Kuopio, Kuopio, FIN-70211, Finland
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(15), 8290-8295
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polyamines are required for optimal growth and function of cells. Regulation of their cellular homeostasis is therefore tightly controlled. The key regulatory enzyme for polyamine catabolism is the **spermidine**/**spermine** N1-acetyltransferase (SSAT). Depletion of cellular polyamines has been associated with inhibition of

growth and programmed cell death. To investigate the physiol. function SSAT, we generated a transgenic rat line overexpressing the SSAT gene under the control of the inducible mouse metallothionein I promoter. Administration of zinc resulted in a marked induction of pancreatic SSAT, overaccumulation of putrescine, and appearance of N1-acetylspermidine with extensive depletion of **spermidine** and **spermine** in transgenic animals. The activation of pancreatic polyamine catabolism resulted in acute **pancreatitis**. In nontransgenic animals, an equal dose of zinc did not affect pancreatic polyamine pools, nor did it induce **pancreatitis**. Acetylated polyamines, products of the SSAT-catalyzed reaction, are metabolized further by the polyamine oxidase (PAO) generating hydrogen peroxide, which might cause or contribute to the pancreatic inflammatory process. Administration of specific PAO inhibitor, MDL72527 [N1,N2-bis(2,3-butadienyl)-1,4-butanediamine], however, did not affect the histol. score of the **pancreatitis**. Induction of SSAT by the polyamine analog N1,N11-diethylnorspermine reduced pancreatic polyamines levels only moderately and without signs of organ inflammation. In contrast, the combination of N1,N11-diethylnorspermine with MDL72527 dramatically activated SSAT, causing profound depletion of pancreatic polyamines and acute **pancreatitis**. These results demonstrate that acute induction of SSAT leads to pancreatic inflammation, suggesting that sufficient pools of higher polyamine levels are essential to maintain pancreatic integrity. This inflammatory process is independent of the production of hydrogen peroxide by PAO.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 225 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:320281 CAPLUS

DOCUMENT NUMBER: 144:429469

TITLE: Genetic manipulation of polyamine catabolism in rodents

AUTHOR(S): Janne, Juhani; Alhonen, Leena; Pietila, Marko; Keinanen, Tuomo A.; Uimari, Anne; Hyvonen, Mervi T.; Pirinen, Eija; Jarvinen, Aki

CORPORATE SOURCE: Department of Biotechnology and Molecular Medicine, A.I. Virtanen Institute for Molecular Sciences, University of Kuopio, Kuopio, FI-70211, Finland

SOURCE: Journal of Biochemistry (Tokyo, Japan) (2006), 139(2), 155-160

CODEN: JOBIAO; ISSN: 0021-924X

PUBLISHER: Japanese Biochemical Society

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Activation of polyamine catabolism through the overexpression of **spermidine/spermine** N1-acetyltransferase (SSAT) in transgenic rodents does not only lead to distorted tissue polyamine homeostasis, manifested as striking accumulation of putrescine, appearance N1-acetylspermidine and reduction of tissue **spermidine** and/or **spermine** pools, but likewise creates striking phenotypic changes. The latter include loss of hair, lipoatrophy and female infertility. Forced expression of SSAT modulates skin, prostate and intestinal carcinogenesis, induces acute **pancreatitis** and blocks early liver regeneration. Although many of these features are directly attributable to altered tissue polyamine pools, some of them are more likely related to the greatly accelerated flux of the polyamines caused by activated catabolism and compensatorily enhanced biosynthesis.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 225 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:552063 CAPLUS

DOCUMENT NUMBER: 141:82364

TITLE: **Spermidine** analogs for prevention and treatment of **pancreatitis** and induction of liver regeneration

INVENTOR(S): Rasanen, Tiina-Liisa; Alhonen, Leena; Sinervirta, Riitta; Keinanen, Tuomo; Herzog, Karl-Heinz; Khomutov,

PATENT ASSIGNEE(S): Alex Radii; Vepsalainen, Jouko; Janne, Juhani
 Tiina-Liisa Rasanen, Finland; Leena Alhonen; Riitta
 Sinervirta; Tuomo Keinanen; Karl-Heinz Herzog; Alex
 Radii Khomutov; Jouko Vepsalainen; Juhani Janne
 Jpn. Kokai Tokkyo Koho, 51 pp.
 SOURCE: CODEN: JKXXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004189714	A2	20040708	JP 2003-33882	20030212
CA 2413720	AA	20040609	CA 2002-2413720	20021209
CA 2452467	AA	20040609	CA 2003-2452467	20031209
US 2004180968	A1	20040916	US 2003-731626	20031209
PRIORITY APPLN. INFO.:			US 2002-431958P	P 20021209
			CA 2002-2413720	A 20021209

OTHER SOURCE(S): MARPAT 141:82364
 AB **Spermidine** analogs (I; R₂R₁N(CR₃R₄)aN(R₁₀)(CR₅R₆)bN(R₁₁) [(CR₇R₈)
 cN(R₁₂)]nR₉ wherein a, b, c = 1-6; n = 0, 1; R₁-R₁₂ = H, alkyl), including
 1-methylspermidine, are claimed for prevention and treatment of
pancreatitis and induction of liver regeneration.

L20 ANSWER 6 OF 225 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:106729 CAPLUS

TITLE: Activated polyamine catabolism in acute
pancreatitis: α -methylated polyamine
 analogues prevent trypsinogen activation and
pancreatitis-associated mortality

AUTHOR(S): Hyvonen, Mervi T.; Herzog, Karl-Heinz; Sinervirta,
 Riitta; Albrecht, Elke; Nordback, Isto; Sand, Juhani;
 Keinanen, Tuomo A.; Vepsalainen, Jouko; Grigorenko,
 Nikolay; Khomutov, Alex R.; Kruger, Burkhard; Janne,
 Juhani; Alhonen, Leena

CORPORATE SOURCE: Department of Biotechnology and Molecular Medicine, A.
 I. Virtanen Institute for Molecular Sciences,
 University of Kuopio, Kuopio, Finland

SOURCE: American Journal of Pathology (2005), Volume Date
 2006, 168(1), 115-122

PUBLISHER: American Society for Investigative Pathology
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Polyamines are essential for normal cellular growth and function.
 Activation of polyamine catabolism in transgenic rats overexpressing
spermidine/spermine N1-acetyltransferase, the key enzyme
 in polyamine catabolism, results in severe acute **pancreatitis**.
 Here, we investigated the role of polyamine catabolism in
pancreatitis and studied the effect of polyamine analogs on the
 outcome of the disease. Polyamine depletion was associated with arginine-
 and caerulein-induced **pancreatitis** as well as with human acute
 necrotizing and chronic secondary **pancreatitis**. Substitution of
 depleted polyamine pools with methylspermidine partially prevented
 arginine-induced necrotizing **pancreatitis** whereas
 caerulein-induced edematous **pancreatitis** remained unaffected.
 Transgenic rats receiving methylated polyamine analogs after the induction
 of **pancreatitis** showed less pancreatic damage than the untreated
 rats. Most importantly, polyamine analogs dramatically rescued the
 animals from **pancreatitis**-associated mortality. Induction of
spermidine/spermine N1-acetyltransferase in acinar cells
 isolated from transgenic rats resulted in increased trypsinogen
 activation. Pretreatment of acini with bismethylspermine prevented
 trypsinogen activation, indicating that premature proteolytic activation
 is one of the effects triggered by polyamine depletion. Our data suggest
 that activation of polyamine catabolism is a general pathway in the
 pathogenesis of acute **pancreatitis** and that exptl. disease can
 be ameliorated with stable polyamine analogs.

REFERENCE COUNT:

31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 225 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:783211 CAPLUS

DOCUMENT NUMBER: 138:331376

TITLE: A Polyamine Analogue Prevents Acute **Pancreatitis** and Restores Early Liver Regeneration in Transgenic Rats with Activated Polyamine Catabolism

AUTHOR(S): Raesaenen, Tiina-Liisa; Alhonen, Leena; Sinervirta, Riitta; Keinaenen, Tuomo; Herzig, Karl-Heinz; Suppola, Suvikki; Khomutov, Alex R.; Vepsaelaeinen, Jouko; Jaenne, Juhani

CORPORATE SOURCE: A.I. Virtanen Institute for Molecular Sciences, University of Kuopio, Kuopio, FIN-70211, Finland

SOURCE: Journal of Biological Chemistry (2002), 277(42), 39867-39872

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We recently generated a transgenic rat model for acute **pancreatitis**, which was apparently caused by a massive depletion of pancreatic polyamines **spermidine** and **spermine** due to inducible activation of their catabolism (Alhonen, L., Parkkinen, J. J., Keinaenen, T., Sinervirta, R., Herzig, K. H., and Jaenne, J. (2000) Proc. Natl. Acad. Sci. U. S. A. 97, 8290-8295). When subjected to partial hepatectomy, these animals showed striking activation of polyamine catabolism at 24 h postoperatively with a profound decrease in hepatic **spermidine** and **spermine** pools and failure to initiate liver regeneration. Here we show that **pancreatitis** in this model could be totally prevented, as judged by histopathol. and plasma α -amylase activity, by administration of 1-methylspermidine, a metabolically stable analog of **spermidine**. Similarly, the analog, given prior to partial hepatectomy, restored early liver regeneration in the transgenic rats, as indicated by a dramatic increase in the number of proliferating cell nuclear antigen-pos. hepatocytes from about 1% to more than 40% in response to the drug. The present results suggest that the extremely high concentration of **spermidine** in the pancreas, in fact the highest in the mammalian body, may have a critical role in maintaining organ integrity. The failure to initiate liver regeneration in the absence of sufficient hepatic polyamine pools similarly indicates that polyamines are required for proper commencement of the regenerative process.

REFERENCE COUNT:

22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

This is Google's cache of <http://www.emedicine.com/EMERG/topic354.htm> as retrieved on Jun 6, 2006 01:57:07 GMT.

Google's cache is the snapshot that we took of the page as we crawled the web.

The page may have changed since that time. Click here for the [current page](#) without highlighting.

This cached page may reference images which are no longer available. Click here for the [cached text](#) only.

To link to or bookmark this page, use the following url: <http://www.google.com/search?q=cache:NUMH3E9n9xQJ:www.emedicine.com/EMERG/topic354.htm+pancreatitis&hl=en&gl=us&ct=clnk&cd=3>

Google is neither affiliated with the authors of this page nor responsible for its content.

These search terms have been highlighted: **pancreatitis**



Know the evaluation and management

Search



[Home](#) | [Specialties](#) | [Resource Centers](#) | [Learning Centers](#) | [CME](#) | [Contributor Recruitment](#)



[Articles](#) [Images](#) [CME](#)

[Advanced Search](#)

June 12, 2006

[Consumer Health](#)

[Link to this site](#)

You are in: [eMedicine Specialties](#) > [Emergency Medicine](#) > [Gastrointestinal](#)

Pancreatitis

Last Updated: March 21, 2005

[Rate this Article](#)

[Email to a Colleague](#)

[Get CME/CE for article](#)

AUTHOR INFORMATION

Section 1 of 9

[Author Information](#) [Introduction](#) [Clinical Differentials](#) [Workup](#) [Treatment](#) [Medication](#) [Follow-up](#) [Bibliography](#)

Author: **Ghattas Khoury, MD**, President, Lebanese Order of Physicians, Clinical Professor, Department of Surgery, American University of Beirut

Coauthor(s): **Samer S Deeba, MD**, Fellow, Department of Surgery, St Mary's Hospital, Imperial College, London

Editor(s): **Jerome FX Naradzay, MD, FACEP**, Medical Director of Emergency Services, Department of Emergency Medicine, Mesa View Regional Hospital; **Francisco Talavera, PharmD, PhD**, Senior Pharmacy Editor, eMedicine

Eugene Hardin, MD, FACEP, FAAEM, Chair and Associate Professor, Department of Emergency Medicine, Charles R Drew University of Medicine and Science; Chair, Department of Emergency Medicine, Martin Luther King, Jr/Drew Medical Center; **John Halamka, MD**, Chief Information Officer, CareGroup Healthcare System

Assistant Professor of Medicine, Department of Emergency Medicine, Beth Israel Deaconess Medical Center

Assistant Professor of Medicine, Harvard Medical School; and **William K Mallon, MD**, Program Director, Internal Medicine, Associate Professor, Department of Emergency Medicine, University of Southern California

Disclosure

INTRODUCTION**Section 2 of 9** [\[Back To Top\]](#)[Author Information](#) [Introduction](#) [Clinical Differentials](#) [Workup](#) [Treatment](#) [Medication](#) [Follow-up](#) [Bibliography](#)

Background: Pancreatitis is an inflammatory process in which pancreatic enzymes autodigest the gland.

The gland can sometimes heal without any impairment of function or any morphologic changes. This process is known as acute **pancreatitis**. It can recur intermittently, contributing to the functional and morphologic loss of the gland. Recurrent attacks are referred to as chronic **pancreatitis**. Both forms of **pancreatitis** are present in the patient with acute clinical findings.

Pathophysiology: Because the pancreas is located in the retroperitoneal space with no capsule, inflammation can spread easily. In acute **pancreatitis**, parenchymal edema and peripancreatic fat necrosis occur first. This process is known as acute edematous **pancreatitis**.

When necrosis involves the parenchyma, accompanied by hemorrhage and dysfunction of the gland, the inflammation evolves into hemorrhagic or necrotizing **pancreatitis**.

Pseudocysts and pancreatic abscesses can result from necrotizing **pancreatitis** because of enzymes being released by granulation tissue (ie, pseudocyst formation) or bacterial seeding of pancreatic or peripancreatic tissue (ie, pancreatic abscess formation). An ultrasound or, preferably, a CT scan can be used to detect both.

The inflammatory process can cause systemic effects because of the presence of cytokines, such as bradykinin and phospholipase A. These cytokines may cause vasodilation, increase in vascular permeability, pain, and leukocyte accumulation in the vessel walls. Fat necrosis may cause hypocalcemia. Pancreatic B cell injury may lead to hyperglycemia.

Frequency:

- **In the US:** Annual incidence of acute **pancreatitis** is 19.5 per 100,000 population and chronic **pancreatitis** is 8.3 per 100,000 population per year.

Mortality/Morbidity:

- Although acute **pancreatitis** should be noted, chronic **pancreatitis** has a more severe presentation as episodes recur.
- Acute respiratory distress syndrome (ARDS), acute renal failure, cardiac depression, hemorrhage, and hypotensive shock all may be systemic manifestations of acute **pancreatitis** in its most severe form.

Race: Annual incidence of acute **pancreatitis** in Native American persons is 4 per 100,000 population, in white persons is 5.7 per 100,000 population, and in black persons is 20.7 per 100,000 population.

Sex: No predilection exists.

Age: The risk for African American persons aged 35-64 years is 10 times higher than for any other group. African American persons are at higher risk than white persons in that same age group.

CLINICAL**Section 3 of 9** [\[Back To Top\]](#)

History:

- The main presentation of acute **pancreatitis** is epigastric pain or right upper quadrant pain radiating to back
- Nausea and/or vomiting
- Fever
- Query the patient about recent surgeries and invasive procedures (ie, endoscopic retrograde cholangiopancreatography) or family history of hypertriglyceridemia.
- Patients frequently have a history of previous biliary colic and binge alcohol consumption, the major cause of acute **pancreatitis**.

Physical:

- Tachycardia
- Tachypnea
- Hypotension
- Fever
- Abdominal tenderness, distension, guarding, and rigidity
- Mild jaundice
- Diminished or absent bowel sounds
- Because of contiguous spread of inflammation (effusion) from the pancreas, lung auscultation may reveal basilar rales, especially in the left lung.
- Occasionally, in the extremities, muscular spasm may be noted secondary to hypocalcemia.
- Severe cases may have a Grey Turner sign (ie, bluish discoloration of the flanks) and Cullen sign (ie, discoloration of the periumbilical area) caused by the retroperitoneal leak of blood from the pancreas in **hemorrhagic pancreatitis**.

Causes:

- The major causes are long-standing alcohol consumption and biliary stone disease.
 - In developed countries, the most common cause of acute **pancreatitis** is alcohol abuse.
 - On the cellular level, ethanol leads to intracellular accumulation of digestive enzymes and triggers premature activation and release.

- On the ductal level, ethanol increases the permeability of ductules, which allow enzymes to the parenchyma, resulting in pancreatic damage.
- Ethanol increases the protein content of the pancreatic juice and decreases bicarbonate to trypsin inhibitor concentrations. This leads to the formation of protein plugs that block the pancreatic outflow and obstruction.
- Another major cause of acute **pancreatitis** is biliary stone disease (eg, cholelithiasis, choledocholithiasis). A biliary stone may lodge in the pancreatic duct or ampulla of Vater and obstruct the pancreatic duct, leading to extravasation of enzymes into the parenchyma.
- Minor causes of acute **pancreatitis**
 - Medications, including azathioprine, corticosteroids, sulfonamides, thiazides, furosemides, NSAIs, mercaptopurine, methyldopa, and tetracyclines
 - Endoscopic retrograde cholangiopancreatography (ERCP)
 - Hypertriglyceridemia (When the triglyceride (TG) level exceeds 1000 mg/U, an episode of **pancreatitis** is more likely.)
 - Peptic ulcer disease
 - Abdominal or cardiopulmonary bypass surgery, which may insult the gland by ischemia
 - Trauma to the abdomen or back, resulting in sudden compression of the gland against the spine posteriorly
 - Carcinoma of the pancreas, which may lead to pancreatic outflow obstruction
 - Viral infections, including mumps, Coxsackievirus, cytomegalovirus (CMV), hepatitis virus, Epstein-Barr virus (EBV), and rubella
 - Bacterial infections, such as mycoplasma
 - Intestinal parasites, such as ascaris, which can block the pancreatic outflow
 - Pancreas divisum
 - Scorpion and snake bites
- Vascular factors, such as ischemia or vasculitis

DIFFERENTIALS

Section 4 of 9 [\[Back To Top\]](#)

[Author Information](#) [Introduction](#) [Clinical Differentials](#) [Workup](#) [Treatment](#) [Medication](#) [Follow-up](#) [Bibliography](#)

[Aneurysm, Abdominal](#)

[Cholangitis](#)

[Cholecystitis and Biliary Colic](#)

[Cholelithiasis](#)

[Gastroenteritis](#)

[Hepatitis](#)[Mesenteric Ischemia](#)[Obstruction, Large Bowel](#)[Obstruction, Small Bowel](#)

Other Problems to be Considered:

Perforated viscus

Acute peritonitis

Choledocholithiasis

Macroamylasemia

Macrolipasemia

Intestinal obstruction

Pancreatic cancer

Malabsorption syndromes/processes

WORKUP

[Author Information](#) [Introduction](#) [Clinical Differentials](#) [Workup](#) [Treatment](#) [Medication](#) [Follow-up](#) [Bibliography](#)

Lab Studies:

- A complete blood count (CBC) demonstrates leukocytosis (WBC >12000) with the differential being shifted polymorphs.
- If blood transfusion is necessary, as in cases of hemorrhagic **pancreatitis**, obtain type and crossmatch.
- Measure blood glucose level because it may be elevated from B cell injury in the pancreas.
- Obtain measurements for BUN, creatine (Cr), and electrolytes (Na, K, Cl, CO₂, P, Mg); a great disturbance in balance is usually found, secondary to third spacing of fluids.
- Measure amylase levels, preferably the Amylase P, which is more specific to pancreatic pathology. Levels higher than normal strongly suggest the diagnosis of acute **pancreatitis**.
- Lipase levels also are elevated and remain high for 12 days. In patients with chronic **pancreatitis** (usually alcohol abuse), lipase may be elevated in the presence of a normal serum amylase level.
- Perform liver function tests (eg, alkaline phosphatase, serum glutamic-pyruvic transaminase [SGPT], serum transaminase [SGOT], G-GT) and bilirubin, particularly with biliary origin **pancreatitis**.

Imaging Studies:

- Perform a plain KUB (Kidneys, ureters, bladder) with the patient in the upright position to exclude viscus (eg, the diaphragm). In cases with a recurrent episode of chronic **pancreatitis**, peripancreatic calcifications may be present.
- Ultrasound can be used as a screening test. If overlying gas shadows secondary to bowel distention are present, the diagnosis is less likely to be **pancreatitis**.
- CT scan is the most reliable imaging modality in the diagnosis of acute **pancreatitis**. The criteria for diagnosis are the presence of peripancreatic fluid, edema, and fat necrosis.

Balthazar and colleagues into 5 grades, as follows:

- Grade A - Normal pancreas
- Grade B - Focal or diffuse gland enlargement
- Grade C - Intrinsic gland abnormality recognized by haziness on the scan
- Grade D - Single ill-defined collection or phlegmon
- Grade E - Two or more ill-defined collections or the presence of gas in or nearby the pancreas
- The use of contrast material intravenously is yet to be proved detrimental on the microcirculation of the necrotizing **pancreatitis**.

Other Tests:

- Para-aminobenzoic acid test (ie, bentiromide [Chymex] test) for chronic **pancreatitis**

TREATMENT

[Author Information](#) [Introduction](#) [Clinical Differentials](#) [Workup](#) [Treatment](#) [Medication](#) [Follow-up](#) [Bibliography](#)

Emergency Department Care: Most of the cases presenting to the ED are treated conservatively, and approach such treatment.

- Fluid resuscitation
 - Monitor accurate intake/output and electrolyte balance of the patient.
 - Crystalloids are used, but other infusions, such as packed red blood cells (PRBCs), are occasionally used in the case of hemorrhagic **pancreatitis**.
 - Central lines and Swan-Ganz catheters are used in patients with severe fluid loss and very low blood pressure.
- Patients should have nothing by mouth, and a nasogastric tube should be inserted to assure an empty stomach at rest.
- Begin parenteral nutrition if the prognosis is poor and if the patient is going to be kept in the hospital for an extended period.
- Analgesics are used to relieve pain. Meperidine is preferred over morphine because of the greater specificity for the sphincter of Oddi.
- Antibiotics are used in severe cases associated with septic shock or when the CT scan indicates that a collection has evolved.
- Other conditions, such as biliary **pancreatitis** associated with cholangitis, also need antibiotic coverage. The antibiotics should be directed against the ones secreted by the biliary system, such as ampicillin and third generation cephalosporins.
- Continuous oxygen saturation should be monitored by pulse oximetry and acidosis should be corrected as soon as possible. If pending respiratory failure develops, intubation should be performed.

- Perform CT-guided aspiration of necrotic areas, if necessary.
- An ERCP may be indicated for common duct stone removal.

Consultations: Consult a general surgeon in the following cases:

- For phlegmon of the pancreas, surgery can achieve drainage of any abscess or scooping of necrotic p followed by postoperative lavage of the pancreatic bed.
- In patients with hemorrhagic **pancreatitis**, surgery is indicated to achieve hemostasis, particularly because eroded in acute **pancreatitis**.
- Patients who fail to improve despite optimal medical treatment or patients who push the Ranson score into the operating room. Surgery in these cases may lead to a better outcome or confirm a different diagnosis.
- In biliary **pancreatitis**, a sphincterotomy (ie, surgical emptying of the common bile duct) can relieve the obstruction. Cholecystectomy may be performed to clear the system from any source of biliary stones.



Targeting Abdominal Obesity to Reduce Cardiovascular Risk in Patients With Type 2 Diabetes

This activity is composed of the following audio/slide presentations:

- Welcome and Program Introduction (Alan D. Cherrington, PhD)
- Why Abdominal Obesity Increases Metabolic and Cardiovascular Risk in Type 2 Diabetes: The Preclinical Evidence (Richard N. Bergman, PhD)
- The Endocannabinoid System: The Mechanisms Behind Metabolic Homeostasis and Imbalance (Stephen C. Woods, PhD)
- Endocannabinoid Blockade for Improving Glycemic Control and Lipids in Patients With Type 2 Diabetes (Priscilla Hollander, MD, PhD)
- Panel Discussion (Moderator Louis J. Aronne, MD, FACP, with panelists Richard Bergman, PhD; Alan D. Cherrington, PhD; Robert R. Henry, MD; Priscilla Hollander, MD, PhD; and Stephen C. Woods, PhD)

TAKE THIS FREE COURSE NOW

MEDICATION

[Author Information](#) [Introduction](#) [Clinical Differentials](#) [Workup](#) [Treatment](#) [Medication](#) [Follow-up](#) [Bibliography](#)

The goal of pharmacotherapy is to relieve pain and minimize complications.

Drug Category: Antibiotics -- Used to cover the microorganisms that may grow in biliary **pancreatitis** and **pancreatitis**. The empiric antibiotic regimen usually is based on the premise that enteric anaerobic and aerobic microorganisms are often the cause of pancreatic infections. Once culture sensitivities are made, adjustments can be done.

Drug Name	Ceftriaxone (Rocephin) -- Third-generation cephalosporin with broad negative activity; lower efficacy against gram-positive organisms; highly resistant organisms. Arrests bacterial growth by binding to one or more proteins.
Adult Dose	1-2 g IM/IV once or divided bid
Pediatric Dose	50-75 mg/kg/d IM/IV divided q12h
Contraindications	Documented hypersensitivity
Interactions	Probenecid may increase levels; coadministration with ethacrynic acid and aminoglycosides may increase nephrotoxicity
Pregnancy	B - Usually safe but benefits must outweigh the risks.
Precautions	Adjust dose in renal impairment; caution in breastfeeding women as it is excreted in breast milk.
Drug Name	Ampicillin (Marcillin, Omnipen) -- Bactericidal activity against susceptible organisms. Alternative to amoxicillin when unable to take medication orally.
Adult Dose	250-500 IM/IV mg q6h
Pediatric Dose	25-50 mg/kg/d IM/IV divided q6-8h
Contraindications	Documented hypersensitivity; viral mononucleosis
Interactions	Probenecid and disulfiram elevate levels; allopurinol decreases effects on ampicillin rash; may decrease effects of oral contraceptives.
Pregnancy	B - Usually safe but benefits must outweigh the risks.
Precautions	Adjust dose in renal failure; evaluate rash and differentiate from hypersensitivity reactions.

Drug Category: Analgesics -- Pain control is essential to quality patient care. It ensures patient comfort, and has sedating properties, which are beneficial for patients who have sustained trauma or have painful lesions.

Drug Name	Meperidine (Demerol) -- Analgesic with multiple actions similar to those of morphine. It produces less constipation, smooth muscle spasm, and depression compared to similar analgesic doses of morphine.
Adult Dose	15-35 mg/h IV; 50-150 mg IM q3-4h
Pediatric Dose	1.1-1.8 mg/kg IM q3-4h
Contraindications	Documented hypersensitivity; MAOIs; upper airway obstruction or respiratory depression; during labor when delivery of premature infant is anticipated.
Interactions	Monitor for increased respiratory and CNS depression with coadministration of hydantoins; may decrease effects; avoid with protease inhibitors.
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Caution in head injuries because may increase respiratory depression (use only if absolutely necessary); caution when using postoperative pulmonary disease (suppresses cough reflex; substantially increase respiratory depression); may aggravate or cause seizures because of tolerance, even if no prior history of seizures; monitor closely for morphine-induced seizure activity if se

FOLLOW-UP

[Author Information](#) [Introduction](#) [Clinical Differentials](#) [Workup](#) [Treatment](#) [Medication](#) [Follow-up](#) [Bibliography](#)

Further Inpatient Care:

- Transfer patients with Ranson scores of 0-2 to a hospital floor.

- Transfer patients with Ranson scores 3-5 to an intensive care unit.
- Transfer patients with Ranson scores higher than 5 to an intensive care unit with emergency surgery if indicated.
- Two other systems, the Acute Physiology and Chronic Health Evaluation (APACHE) and the Multiple Organ Failure Score (MOFS), have been used recently, but these are used more in an ICU setting.

Further Outpatient Care:

- The patient should be followed routinely with physical examination and amylase and lipase assays.

Complications:

- Infected pancreatic necrosis may result from seeding of bacteria into the inflammation.
- An acute pseudocyst is an effusion of pancreatic juice that is walled off by granulation tissue after an episode of necrosis.
- Hemorrhage into the GI tract retroperitoneum or the peritoneal cavity is possible because of erosion of the pancreatic duct.
- Intestinal obstruction or necrosis may occur.
- Common bile duct obstruction may be caused by a pancreatic abscess, pseudocyst, or biliary stone that has migrated.
- An internal pancreatic fistula from pancreatic duct disruption or a leaking pancreatic pseudocyst may cause a fluid collection.

Prognosis:

- Ranson developed a series of different criteria for the severity of acute **pancreatitis**.
 - Present on admission
 - Older than 55 years
 - WBC higher than 16,000 per mcL
 - Blood glucose higher than 200 mg/dL
 - Serum lactate dehydrogenase (LDH) more than 350 IU/L
 - SGOT (ie, aspartate aminotransferase [AST]) greater than 250 IU/L
 - Developing during the first 48 hours
 - Hematocrit fall more than 10%
 - BUN increase more than 8 mg/dL
 - Serum calcium less than 8 mg/dL
 - Arterial oxygen saturation less than 60 mm Hg

- Base deficit higher than 4 mEq/L
- Estimated fluid sequestration higher than 600 mL
- A Ranson score of 0-2 has a minimal mortality rate.
- A Ranson score of 3-5 has a 10%-20% mortality rate.
- A Ranson score higher than 5 has a mortality rate of more than 50% and is associated with more systemic complications.

Patient Education:

- Educate patients about the disease and advise them to avoid alcohol in binge amounts and to discontinue fatty meals and abdominal trauma.
- For excellent patient education resources, visit eMedicine's [Liver, Gallbladder, and Pancreas Center](#). / education article, [Pancreatitis](#).

BIBLIOGRAPHY

[Author Information](#) [Introduction](#) [Clinical Differentials](#) [Workup](#) [Treatment](#) [Medication](#) [Follow-up](#) [Bibliography](#)

- Calleja GA, Barkin JS: Acute **pancreatitis**. Med Clin North Am 1993 Sep; 77(5): 1037-56[[Medline](#)].
- Moscati RM: Cholelithiasis, cholecystitis, and **pancreatitis**. Emerg Med Clin North Am 1996 Nov; 14(4): 831-52[[Medline](#)].
- Plock JA, Schmidt J, Anderson SE, et al: Contrast-enhanced computed tomography in acute **pancreatitis**: does it worsen its course due to impaired microcirculation?. Langenbecks Arch Surg 2005 Feb 12;[[Medline](#)].
- Schwartz Gr, et al: Acute **pancreatitis**. In: Principles and Practice of Emergency Medicine. Vol 2. 1997.
- Steer ML: Classification and pathogenesis of **pancreatitis**. Surg Clin North Am 1989 Jun; 69(3): 467-86[[Medline](#)].
- Taylor SL, Morgan DL, Denson KD, et al: A comparison of the Ranson, Glasgow, and APACHE II scoring systems for organ system score in predicting patient outcome in **pancreatitis**. Am J Surg 2005 Feb; 189(2): 219-25[[Medline](#)].
- Trede M, Carter DC: Acute **pancreatitis**. In: Surgery of the Pancreas. 1993: 161-259.
- Werner J, Feuerbach S, Uhl W, Buchler MW: Management of acute **pancreatitis**: from surgery to intensive care. Ann Surg 2005 Mar; 241(3): 426-36[[Medline](#)].

NOTE:

Medicine is a constantly changing science and not all therapies are clearly established. New research changes drug and treatment therapies daily. The authors, editors, and publishers of this publication make every effort to provide information that is up-to-date and accurate and is generally accepted within medical standards at the time of publication. However, as medical science is always changing, the authors, editors, and publisher or any other party involved with the publication of this article do not warrant the information in this article is accurate or complete. The reader should confirm the information in this article from other sources prior to use. In particular, contraindications should be confirmed in the package insert. **FULL DISCLAIMER**

Pancreatitis excerpt

[About Us](#) | [Privacy](#) | [Terms of Use](#) | [Contact Us](#) | [Advertise](#) | [Institutional Subscribers](#)



We subscribe to the
[HONcode principles](#) of the
Health On the Net Foundation

© 1996-2006 by WebMD
All Rights Reserved